

## II. REMARKS

### Formal Matters

Claims 1, 3, 5-18, and 23-28 are pending after entry of the amendments set forth herein.

Claims 1-4 and 19-22 were examined and were rejected. Claims 5-18 and 23-28 were withdrawn from consideration.

Claims 1 and 3 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1 and 3 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 14, lines 31-33; and Table 9. Accordingly, no new matter is added by these amendments.

Claims 2, 4, 19-22, and 29 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

### PTO SB-08A form

Applicants respectfully request that the Examiner initial and return the PTO SB-08A form submitted with the Information Disclosure Statement filed on December 13, 2004 in this application, thereby indicating that the references cited therein have been reviewed and made of record.

### Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-4, 19-22, and 29 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Claims 2, 4, 19-22, and 29 are canceled without prejudice to renewal, thereby rendering this rejection of these claims moot.

Claims 1 and 3 are amended to recite a pharmaceutical composition comprising a disulfonate and a pharmaceutically acceptable excipient.

Applicants have provided a description of compounds that inhibit apoE4 domain interaction. Specification, page 12, line 11 to page 15, line 3; Example 7; and Table 9. Included among these compounds is a disulfonate, an example of which is azocarmine G, as shown in Example 7 and Table 9. Applicants have provided ample description of how to determine whether a give compound inhibits apoE4 domain interaction. Specification, page 12, line 11 to page 15, line 33; and Example 7. Thus, the instant specification provides ample description, including a working example, of pharmaceutical compositions comprising disulfonate compounds that inhibit apoE4 domain interactions. Accordingly, claims 1 and 3 meet the enablement requirement of 35 U.S.C. §112, first paragraph.

Applicants submit that the rejection of claims 1-4, 19-22, and 29 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

#### Rejection under 35 U.S.C. §102(a)

Claims 1-4 and 19-22 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by Scolnick (WO 95/06470). The Office Action stated that claims 1-4 and 19-22 were rejected over Scolnick for reasons of record stated in the Office Action dated March 18, 2003.

#### Comments regarding the instant invention as claimed

Claim 1 recites a pharmaceutical composition comprising (a) a disulfonate, wherein the disulfonate binds specifically to apolipoprotein E4 (apoE4) and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%; and (b) a pharmaceutically acceptable excipient.

ApoE contains two structural domains: an amino-terminal domain and a carboxyl-terminal domain. Each domain is associated with a specific function. The amino-terminal domain contains the lipoprotein receptor binding region; and the carboxyl-terminal domain contains the major lipid-binding elements. The two domains appear to interact with each other in an isoforms-specific manner, a phenomenon known as “domain interaction.” Domain interaction is responsible for the preference of apoE4 for very low density lipoproteins. The properties of apoE4 are associated with various pathologies, including Alzheimer’s Disease. The present invention provides compounds that bind to apoE4 and reduce domain interaction. Such compounds effect a change in the conformation of apoE4 from a pathological conformation to a non-pathological conformation.

Comments regarding claim amendments

Claims 1 and 3 are amended to recite a pharmaceutical composition comprising a disulfonate and a pharmaceutically acceptable excipient. Claims 2, 4, 19-22, and 29 are canceled without prejudice to renewal, thereby rendering this rejection of these claims moot.

Scolnick cannot anticipate the instant invention as claimed.

The final Office Action stated: 1) Scolnick discloses that a HMG-CoA reductase inhibitor, a statin such as lovastatin, simvastatin, pravastatin, and fluvastatin, being an agent that specifically reduces apolipoprotein E4, is useful in a composition to be administered or a pharmaceutical formulation; and 2) these statins are known to have molecular weights in a range within the instant claim. The Office Action concluded that Scolnick anticipates the claimed invention. Applicants respectfully traverse the rejection.

It is basic patent law that in order to anticipate a claim, a reference must teach each and every element of the claim. *Verdegaal Bros. v. Union Oil of California*, 2USPQ2d 1051, 1053 (Fed. Cir. 1987).

Scolnick discusses statin compounds. The statin compounds discussed in Scolnick are not disulfonates. Scolnick neither discloses nor suggests a pharmaceutical composition comprising a disulfonate and a pharmaceutically acceptable excipient, wherein the disulfonate specifically binds to apoE4 and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%. Accordingly, Scolnick cannot anticipate claims 1 and 3.

Conclusion as to the rejection under 35 U.S.C. §102(a)

Applicants submit that the rejection of claims 1-4 and 19-22 under 35 U.S.C. §102(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.


### III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-096CIP3.

Respectfully submitted,  
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